

CEPI

CEPI's Approach to Standards, Assays & Animal Models

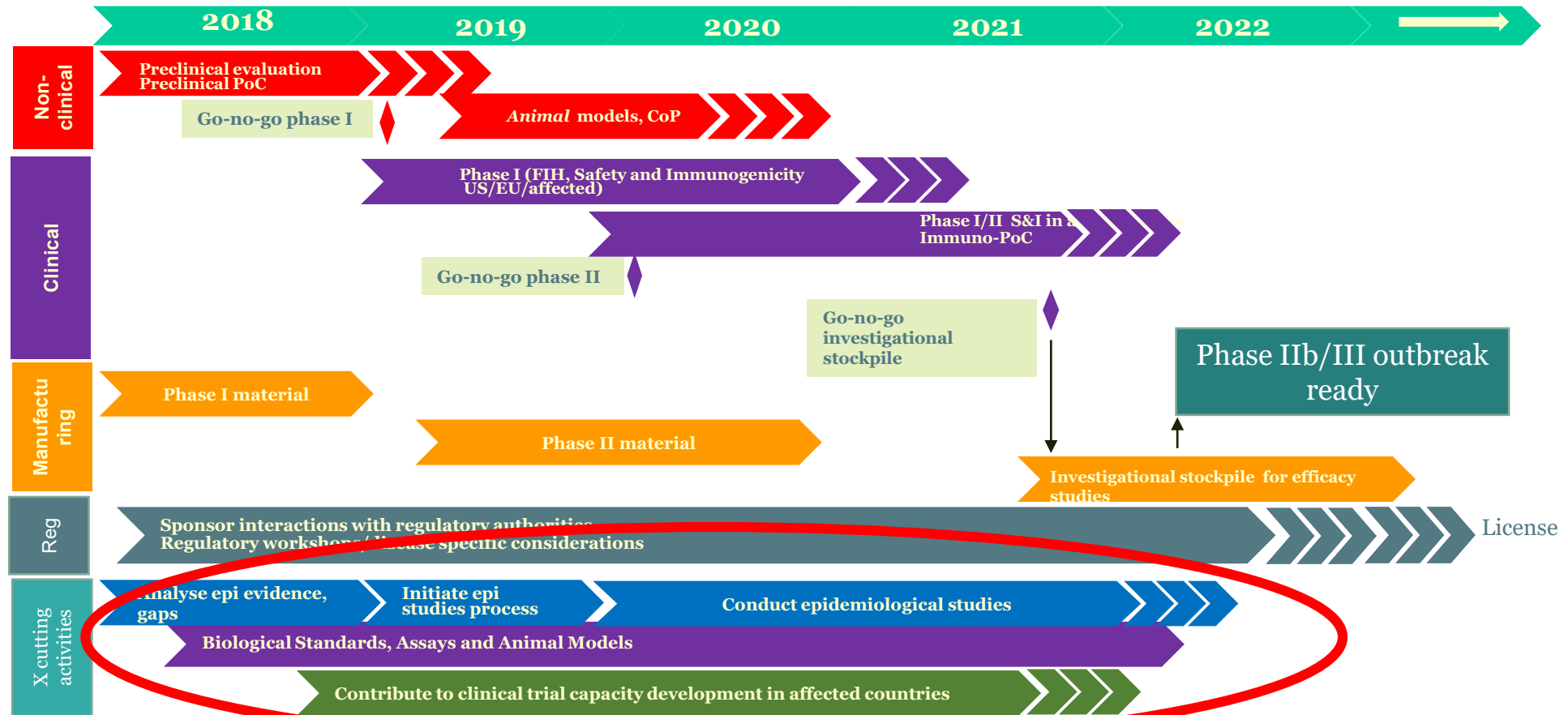
Accra, Ghana; 9th November 2018

Johan Holst, CEPI-Secretariat, Oslo



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Facilitating Accelerated Vaccine Development



PoC: Proof of Concept
 CoP: Correlate of protection
 S&I: Safety and immunogenicity

Aims

Biological Standards, Assays and Animal Models

- Enable comparable immunogenicity testing: providing human convalescent sera and manufacture antigens of optimal confirmation for all diseases of interest to CEPI
- Develop Interim Standards as early as possible (collaborative studies)
- All CEPI Vaccine Development Projects use same Reference Materials (Standards)
- Consensus for assays to measure vaccine response (SOPs + Regulatory inputs)
- Compare subsets of sera from vaccinees evaluated “Head-to-Head” by external lab
- Same/similar animal model to be used; at minimum the same challenge strain

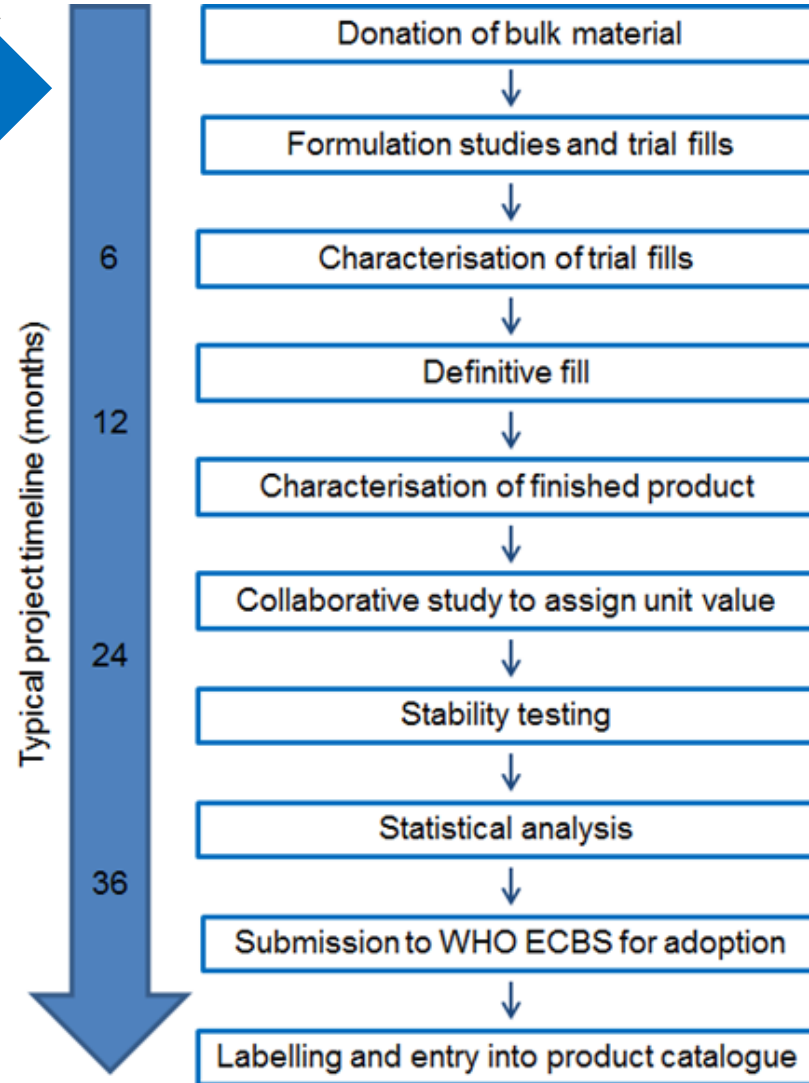
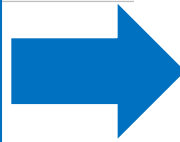
International Biological Standards

- **Their use enables:**
 - Calibration and harmonization of assay data; -consistency in measurement of biological activity
 - Development of internationally agreed criteria for production and control of biological products
 - Comparison of data (e.g. immunogenicity data) from different sources and/or different products
- Support assay establishment, product development and facilitate licensure. Also needed for on-going quality control throughout product life cycle.
- Needed as early as possible for vaccine evaluation and development of potential correlates of protection.
- Play a key role in facilitating the transfer of laboratory science and products into clinical practice, but can take up to three years to develop. Will always involve collaborative studies in many laboratories (5-25)

Development, Characterization and Establishment of Biological Standards

Project endorsement

- Coordinating Laboratory
- WHO, ECBS



CEPI's Working Group on Biological Standards, Assays and Animal Models

Co-chaired by the WHO (**Emer Cooke**) and CEPI (**Johan Holst**)

WG member	Institution
Barbara Schnierle	Paul-Ehrlich Institute (PEI), Germany
Mark Page	National Institute of Biological Standardization and Control (NIBSC), UK
Patricia Aprea	Instituto Nacional de Medicamentos (INAME)), Argentina
Robin Levis	Centre for Biologics Evaluation and Research (CBER), USA
Peter Horby	ISARIC/Univ. of Oxford, UK
James Southern	Chair Developing Country Vaccine Regulators' Network (DCVRN), South-Africa

Coordination and analysis; CEPI-Secretariat by Trygve Danielsen, Raul Gomez Roman, Mike Whelan, Elwyn Griffiths

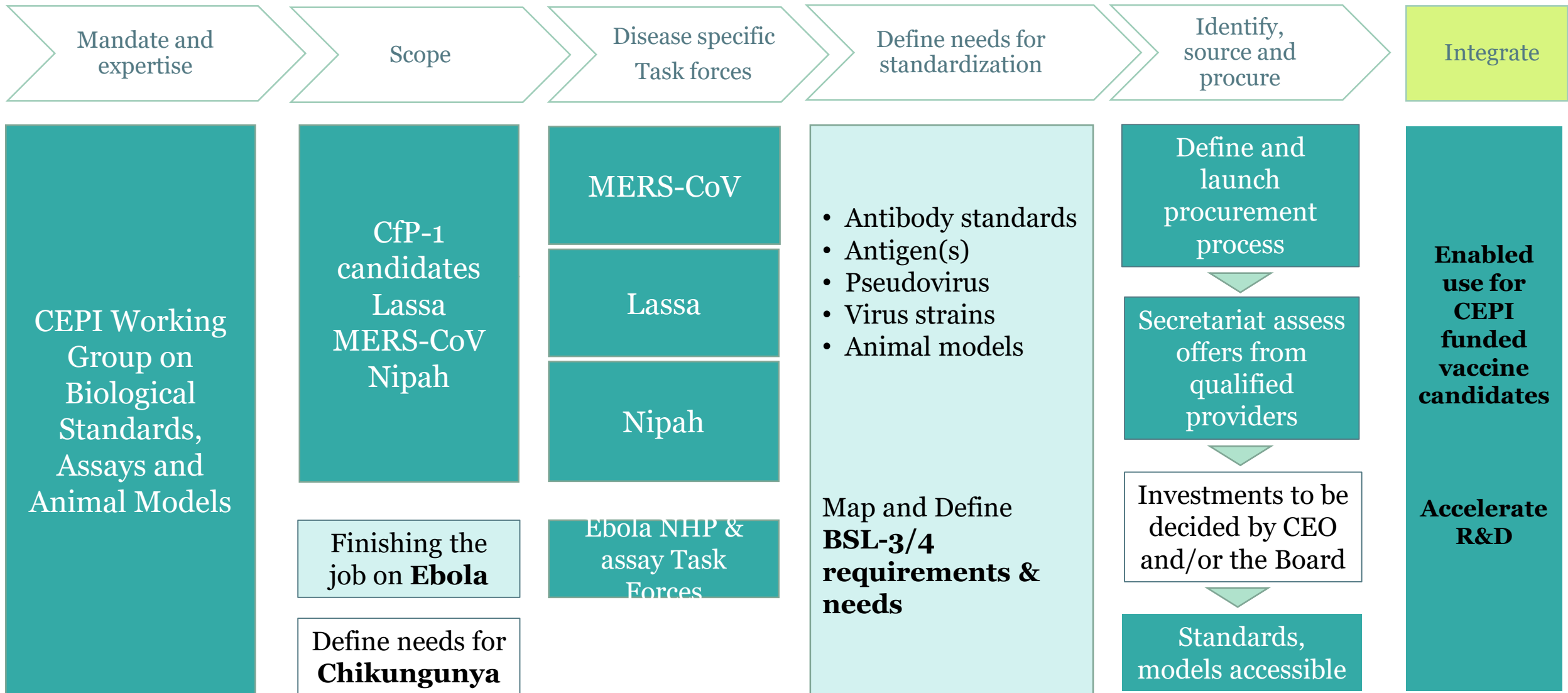
Responsibilities of the Working Group

Objective

Define the need, specifications and approach for developing Biological Standards, Assays and Animal Models for CEPI's Vaccine Development programs

- Outline/expand key steps in the process
- Clarify roles and capabilities of various actors in this space
- Identify goals and challenges for development of standards and models
- Propose approaches for achieving access for CEPI funded vaccine developers
- Facilitate interaction with regulatory expertise and discuss the best approach towards licensure for CEPI's prioritized Vaccines

Biological Standards, Assays and Animal Models



Task Force for Lassa Standards & Assays

Members:

Christian Happi, Igor S. Lukashevich, Erica Ollmann Saphire, Larry Wolfraim, Stephan Günther, Mark Page, Ivana Knezevic, Roland Tschismarov (Themis Bioscience GmbH), Jean Bover (Inovio Pharmaceuticals), Jill Gilmour (IAVI), Rong Xu (Profectus Biosciences).

Deliverables:

- 1. Landscaping** - Report by December 2018.
- 2. Recommendations** - Ab & Ag Standards RfP - June 2018.
- 3. Consensus on key assay(s)** - Q2 2019
- 4. Vaccine characterization & immuno analysis** - Advise on laboratories for this.
- 5. Plan & organize meetings** - Discuss assays, compare results, advise on vaccine evaluation.

Lassa Standards; Request for Proposals (RfP)

- Recombinant Antigen(s): NP (Nucleoprotein) and GPC (Glycoprotein Precursor Complex)
- Serum from Lassa Survivors
 - a) *Additional data collection*
 - b) *Longitudinal follow-up*
 - c) *Multi-country/clade collection*
 - d) *Additional sample collection/Provision of sera to relevant groups*
- Development of these two into Interim Biological Standards
 - a) *Development towards International Reference Preparations (IRPs)*

Submissions and timeline for Lassa Biostandards

- Recombinant Antigen : 4
- Serum from Lassa survivors : 6
- Dev. of Interim Biological Standards : 2

- **Total Projects : 12**
- **Total Applicants : 9**



Lassa Biostandards – Expected Outcomes

- Recombinant NP and GPC from clade II and IV
- Serum panels (low, medium and high titer) from different clades (II-V)
- Serum suitable for the development of a biological standard
 - **Interim Ab standard available from January 2020**
 - Scope might change during the projects; pending new information about reactivity and (potential) cross-clade protection

Next Steps

- Finalize Lassa Biostandards procurement; Define key assays & develop SOPs
- Optional Work Packages suitable for other type of funding (Epi-Studies etc.)
- Launch similar process for Nipah; contracts signed February/March 2019
- Start up MERS-CoV Task Force November 2018; launch RfP process spring 2019
- Plan Face-to-Face meetings for the Task Forces; Discussion of assays, standards and animal models based on actual data, incl. Reg.-input; spring 2019
- Particular attention to Landscaping for Animal Models for Lassa, Nipah and MERS needed. Both regarding harmonization and BSL-3/4 capacity
- Workshops summer/autumn 2019 for linking Standards, Assays & Animal Models to Regulatory Science per priority disease

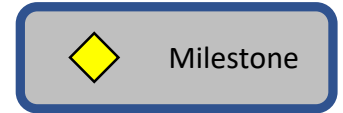
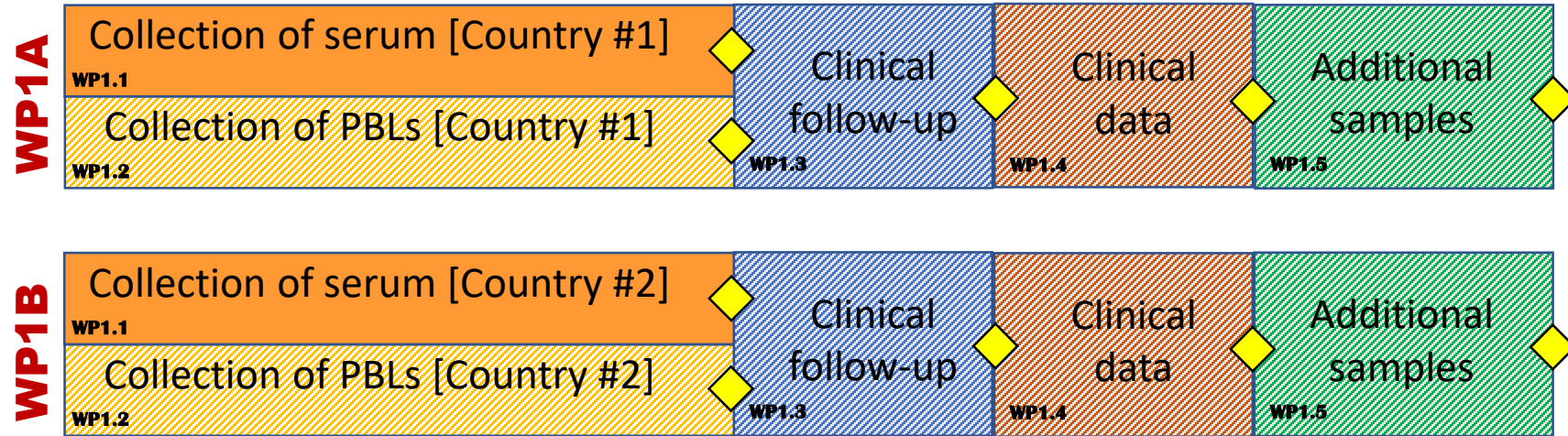
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Back Up Slides

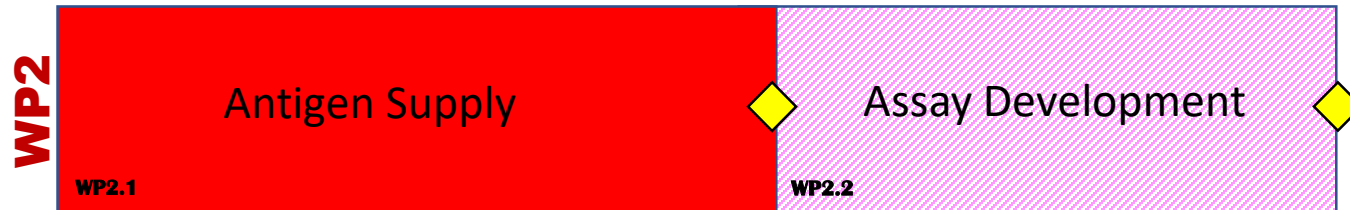
Development, Characterization and Establishment of Biological Standards

- Principles for the development of a biological standard include:
 - Comparable behaviour of a test sample in relation to a standard (ref.)
”**like versus like**”
 - Intended use and users
 - Value assignment in arbitrary (IU) rather than absolute units (SI)
 - Value assignment based upon a variety of relevant methods; so that the definition of IU is not (usually) dependent on a specific method of determination
 - Reflects “state of the art” at time of donation of candidate material

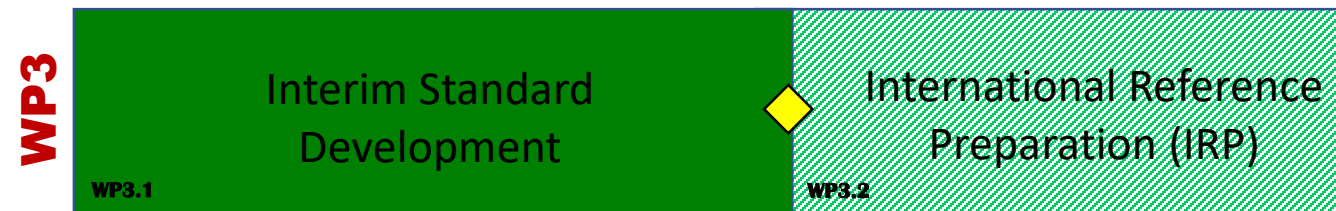
Optimised Work Package structure for Standards&Assays



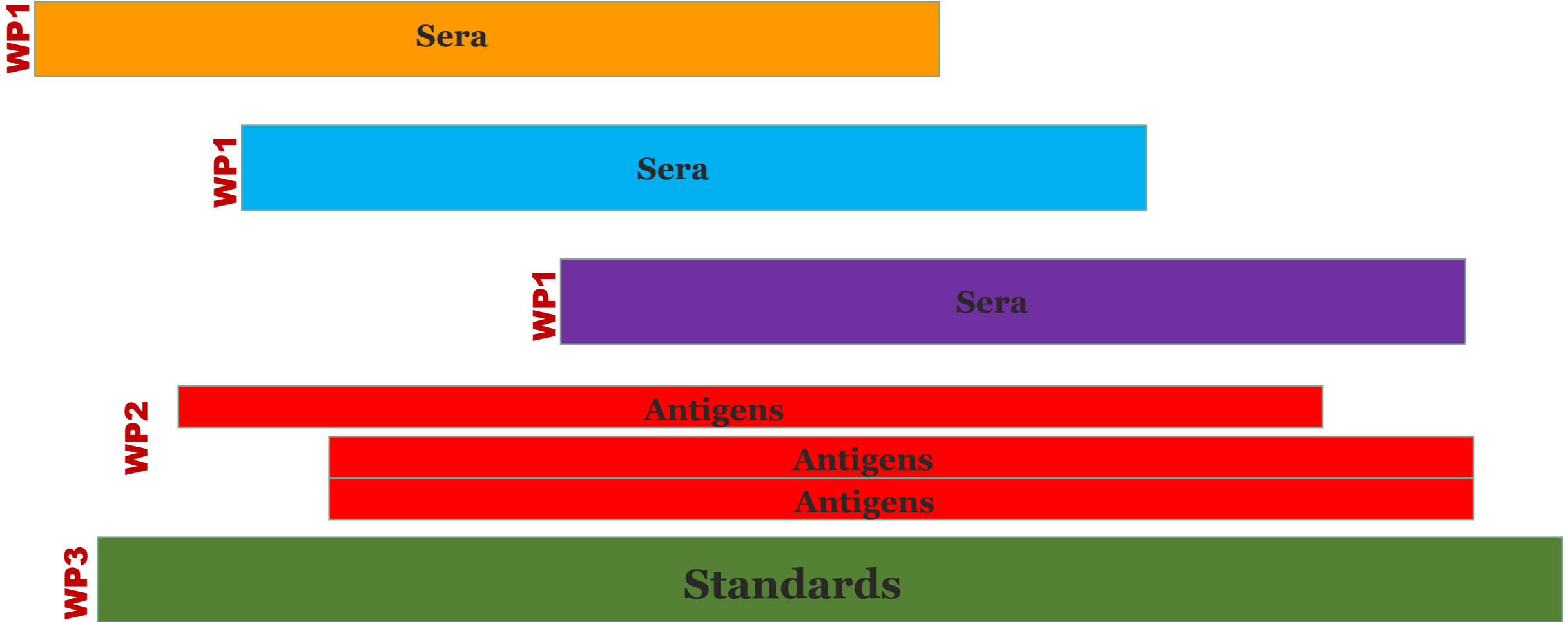
Please note that hashed cells represent optional work-packages



- The Integrated Standards Development Plan (iSDP) will be held by CEPI
- Awardees will carry out one (or more) of the work-packages (WP)
- Overall control will be held by CEPI who will ensure that all topics are adequately covered
- A Team Charter will exist for each consortium
- A Project Team Charter will combine all partners to encompass the entire work plan and will be held by CEPI



Lassa, Nipah & MERS



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Confidential

Fast Track for Ebola Standards

- Recent projects to establish reference reagents for Ebola virus showed that both NIBSC and WHO can respond rapidly to an emerging threat
- Five reference reagents/run controls were developed and established in ~12months (**initially as Interim Standards**)



The screenshot shows a web browser window displaying a GOV.UK press release. The URL in the address bar is <https://www.gov.uk/government/news/nibsc-ebola-reference-reagents-endorsed-as-global-standards-by-who>. The page features the GOV.UK logo and a search bar. The main heading is "NIBSC Ebola reference reagents endorsed as global standards by WHO". Below the heading, it states "From: Medicines and Healthcare products Regulatory Agency" and "First published: 5 November 2015". The text of the press release reads: "The Ebola reference reagents produced by NIBSC and endorsed by the WHO Expert Committee on Biological Standardisation can now be used in laboratory tests by the scientific community." There is a small image of Ebola virus particles. Below the image, it says: "Ebola reference reagents produced by the National Institute for Biological Standards and Control (NIBSC) have been endorsed as the global standards for use in laboratory tests by the World Health Organisation (WHO) Expert Committee on Biological Standardisation and are now available to the scientific community." At the bottom, it mentions: "NIBSC was asked by WHO to produce 2 types of Ebola reference reagents. The first is run alongside patient samples to detect Ebola infection. The